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PATENT
Our Docket: P-IX 1655

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:
Kauffman and Ballivet

Serial No.: 08/464,141

Filed: June 5, 1995

For: PROCESS FOR OBTAINING DNA, RNA, PEPTIDES, POLYPEPTIDES, OR PROTEIN BY RECOMBINANT DNA TECHNIQUE

Group Art Unit: 1805

Examiner: T. Wai

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on May 24, 1996.

By _____
David A. Gay

May 24, 1996
Date of Signature

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

RESPONSE TO OFFICE ACTION

This Amendment is submitted in response to the Office Action mailed November 24, 1995, in connection with the above-identified application. Applicants respectfully request entry of the following amendments and consideration of remarks below.

AMENDMENTS

IN THE CLAIMS:

In claim 1, line 3, before "stochastic" insert --a population of--.

In claim 1, line 5, delete the word "such" and substitute therefor the phrase --said population of--.

In claim 1, line 9, delete the word "such" and substitute therefor --said--.

2. (Amended) A process for the production of a peptide, polypeptide, or protein having a predetermined property, comprising the steps of:

producing a population of at least partially stochastic synthetic polynucleotide sequences,

introducing the population of at least partially stochastic polynucleotide sequences thus obtained into host cells to produce transformed host cells;[,]

cultivating the transformed host cells containing [these] the population of at least partially stochastic polynucleotide sequences so as to clone the stochastic polynucleotide sequences [so as to clone the stochastic polynucleotide sequences] and lead to the production of peptides, polypeptides, or proteins expressed by at least some of these stochastic polynucleotide sequences;[,]

carrying out screening and/or selection methods on said [such] clones of transformed host cells to identify those clones producing the peptide, polypeptide, or protein having the predetermined property;[,]

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isolating the clones so identified, and

growing the isolated clones in a manner so as to produce the peptide, polypeptide, or protein having the predetermined property.

In claim 67, line 2, after "1" insert --or 2--.

REMARKS

Claims 1, 2 and 67 are pending in the present application. All claims have been amended above. The language of the present claims is believed to be responsive to the issues raised in the Office Action. Support for the amendments can be found throughout the specification. Specifically, support for the amendment to "diverse populations" is inherent in the specification and can, for example, also be found on page 1, lines 15-22. The amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Applicants thank the Examiner for acknowledging receipt of a certified copy of the priority document and that it has been filed in the parent application 06/942,630.

Applicants traverse all grounds of rejections for the reasons which follow. The present invention provides a process

for the production of a peptide, polypeptide or protein having a predetermined property. The methods are advantageous in that they allow the construction and screening of a population of unknown sequences for a particular peptide, polypeptide or protein having a predetermined property of interest. The methods consist of first producing a population of polynucleotide sequences comprising stochastically generated sequences which encode a population of peptides, polypeptides or proteins and then screening this population to identify the molecule having the predetermined property of interest. Once identified, the encoding polynucleotide sequence can be isolated, sequenced and used to produce the peptide, polypeptide or protein exhibiting the predetermined property of interest. Methods for utilizing the peptide, polypeptide or protein exhibiting the predetermined property for the detection or titration of a ligand are also provided.

PROVISIONAL REJECTIONS

Claims 1, 2, and 67 stand provisionally rejected under 35 U.S.C. § 101 as allegedly claiming the same invention as that of claims 1, 2 and 67 of copending application Serial No. 08/468,468. Applicants respectfully request to defer responding to this provisional ground of rejection since there has been no indication of allowable subject matter. At the time one or more

allegedly conflicting claims are indicated to be allowable, Applicant will then appropriately respond to this ground of rejection.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1, 2 and 67 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Briefly, the Office Action alleges that the specification lacks guidance and that there is no predictability in producing a functional protein with desired properties from stochastically generated sequences. Therefore, undue experimentation would be required to practice the invention as claimed.

Applicants contend that undue experimentation is not required to practice the invention as claimed. The above-identified application is a continuation application of serial no. 08/349,510. Both the above-identified application and the parent application are being examined by the same Examiner. In the parent application, the identical rejection to that set forth above under 35 U.S.C. § 112, first paragraph was also set forth during the prosecution of that application. Applicants interviewed the parent application and presented remarks sufficiently persuasive to remove the present rejection under 35 U.S.C. § 112, first paragraph. Since there appears to be no

distinction between this rejection in the parent application and that set forth in the above-identified application, Applicants believe that the same arguments presented in the parent application will apply to the present rejection. Therefore, Applicant will set forth for the record those remarks discussed in the personal interview conducted in the parent application.

Applicants contend that the specification provides adequate guidance for one skilled in the art to practice the invention as claimed. Specifically, the invention is not directed to the production of a [single] protein having a predetermined property as stated in the Office Action. Instead, the invention is directed to the production of a population of peptides, polypeptides or proteins and then screening that population to find a peptide, polypeptide or protein having a predetermined property. No guidance or predictability is necessary for producing a single functional peptide, polypeptide or protein having a predetermined property because the invention is not directed to such a method. Instead, the specification teaches those skilled in the art how to make and screen a population of peptides, polypeptides or proteins in order to identify one molecule within that population which exhibits the predetermined property. Applicants have amended the claims above so that the methods now recite the production and screening of a

population of stochastic sequences. Therefore, Applicants respectfully request that this ground of rejection be removed.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1, 2 and 67 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Sirotkin, U.S. Patent No. 4,959,312. The Office Action alleges that Sirotkin describes a method of producing random sequences using terminal transferase and a method that produces mutants containing random substitution mutations at random sites.

Sirotkin is directed to the mutagenesis of a known target DNA. The mutagenesis methods described by Sirotkin result in a single randomly-located region in the target DNA with random substitution mutations. This mutagenesis is accomplished by adding two non-complementary nucleotides to a primer and then incorporating these nucleotides into the template strand. The incorporation of these two nucleotides results in the mutation of the codon at that particular position and the substitution of a different amino acid.

Applicants contend that Sirotkin does not teach or suggest the invention as claimed. Applicants claim a process comprising the production of a population of stochastic or

partially stochastic polynucleotide sequences. Such populations are diverse in sequence and complexity and are produced by, for example, the random copolymerization or chemical coupling of nucleotide monomers. Applicants claimed method does not utilize a template molecule nor does it result in substitution mutations within a single randomly-located region within the target DNA. Therefore, the methods described by Sirotkin do not result in or even suggest the production of stochastic sequences as presently claimed and cannot anticipate the invention. Absent such a description, Sirotkin cannot anticipate the invention as presently claimed.

Finally in regard to claim 67, Sirotkin does not teach or suggest the use of a stochastic or partially stochastic sequence for the detection or titration of a ligand. The mutagenesis described by Sirotkin is directed to identifying and characterizing the correlation between structure and function. Therefore, the passage cited in the Office Action (column 1, lines 38-47) is directed to studies which involve a deliberate change in the protein of interest and then assessing whether the know activity of that protein is changed. There is no utilization of a protein for detecting or titrating a ligand. Moreover, there is no teaching or suggestion for the utilization of a stochastic or partially stochastic protein for detecting or

titrating a ligand. Absent such teachings, Sirotkin cannot anticipate the invention as claimed.

In light of the above remarks, Applicants believe they have adequately distinguished the claimed invention from the cited art. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

CONCLUSION

In light of the foregoing amendments and remarks, Applicants respectfully request withdrawal of all rejections and solicit an allowance of the pending claims. The Examiner is invited to contact Cathryn Campbell or the undersigned agent at (619) 535-9001 if there are any remaining issues to be resolved.

Respectfully submitted,

Date: May 24, 1996

David A. Gay
Registration No. 39,200
Telephone No.: (619) 535-9001
Facsimile No.: (619) 535-8949

CAMPBELL AND FLORES
4370 La Jolla Village Drive
Suite 700
San Diego, California 92122